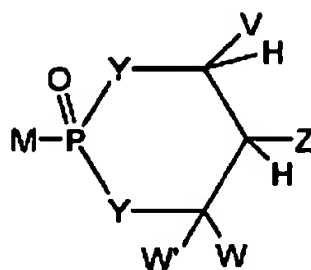


Patent
45198.00013.RCE2

CLAIMS

A complete set of all claims previously submitted, including the status for each claim, immediately follows below.

1. (Previously Amended) A compound of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Patent
45198.00013.RCE2

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p\text{-OR}^{12}$, and $-(\text{CH}_2)_p\text{-SR}^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-\text{R}^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

one Y is -O- and the other Y is $-\text{NR}^6$ -;

M is selected from the group that attached to PO_3^{2-} , $\text{P}_2\text{O}_6^{3-}$, $\text{P}_3\text{O}_9^{4-}$ or $\text{P}(\text{O})(\text{NHR}^6)\text{O}^-$ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not $-\text{NH}(\text{lower alkyl})$, $-\text{N}(\text{lower alkyl})_2$, $-\text{NH}(\text{lower alkylhalide})$, $-\text{N}(\text{lower alkylhalide})_2$, or $-\text{N}(\text{lower alkyl})(\text{lower alkylhalide})$; and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

2. (Previously Amended) The compounds of claim 1 wherein $\text{MP}(\text{O})(\text{NHR}^6)\text{O}^-$, MPO_3^{2-} , $\text{MP}_2\text{O}_6^{3-}$, or $\text{MP}_3\text{O}_9^{4-}$ is selected from the group consisting of an antiviral, anticancer, antihyperlipidemic, antifibrotic, and antiparasitic agent.

Patent
45198.00013.RCE2

3. (Previously Amended) The compound of claim 1 wherein $\text{MP}(\text{O})(\text{NHR}^6)\text{O}^-$, MPO_3^{2-} , $\text{MP}_2\text{O}_6^{3-}$, or $\text{MP}_3\text{O}_9^{4-}$ is selected from the group consisting of metalloprotease inhibitor and TS inhibitor.

4. (Currently Amended) The compounds of claim 1742 wherein MH is selected from the group consisting of LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC, ribavirin, penciclovir, 5-fluoro-2'-deoxyuridine, FIAU, FIAC, BHCG, 2'R,5'S(-)-1-[2-(hydroxymethyl)oxathiolan-5-yl]cytosine, (-)-b-L-2',3'-dideoxycytidine, (-)-b-L-2',3'-dideoxy-5-fluorocytidine, FMAU, BvaraU, E-5-(2-bromovinyl)-2'-deoxyuridine, Cobucavir, TFT, 5-propynyl-1-arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'-deoxyguanosine, Cytallene, Oxetanocin A, Oxetanocin G, Cyclobut A, Cyclobut G, fluorodeoxyuridine, dFdC, araC, bromodeoxyuridine, IDU, CdA, F-araA, 5-FdUMP, Coformycin, and 2'-deoxycophomycin.

5. (Currently Amended) The compounds of claim 1742 wherein MH is selected from the group consisting of ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

6. (Currently Amended) The compounds of claim 174 wherein MPO_3^{2-} is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMPA, FMPA, and PMPA.

7. (Original) The compounds of claim 3 wherein M is attached to the phosphorus in formula I via an oxygen atom that is in a hydroxyl group on an acyclic sugar group.

8. (Original) The compounds of claim 7 wherein MH is selected from the group consisting of ACV, GCV, 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, and (R)-9-(3,4-dihydroxybutyl)guanine.

9. (Original) The compounds of claim 1 wherein M is attached to the phosphorus in formula I via a carbon atom.

10. (Original) The compounds of claim 9 wherein M-PO_3^{2-} is selected from the group consisting of phosphonoformic acid, and phosphonoacetic acid.

Patent
45198.00013.RCE2

11. (Original) The compounds of claim 1 wherein $\text{MP}(\text{O})(\text{NH R}^6)\text{O}^-$, MPO_3^{2-} , $\text{MP}_2\text{O}_6^{3-}$, or $\text{MP}_3\text{O}_9^{4-}$ is useful for the treatment of diseases of the liver or metabolic diseases where the liver is responsible for the overproduction of a biochemical end product.

12. (Original) The compounds of claim 11 wherein said disease of the liver is selected from the group consisting of hepatitis, cancer, fibrosis, malaria, gallstones, and chronic cholecystolithiasis.

13. (Original) The compounds of claim 12 wherein MPO_3^{2-} , $\text{MP}_2\text{O}_6^{3-}$, or $\text{MP}_3\text{O}_9^{4-}$ is an antiviral or anticancer agent.

14. (Original) The compounds of claim 11 wherein said metabolic disease is selected from the group consisting of diabetes, atherosclerosis, and obesity.

15. (Original) The compounds of claim 11 wherein said biochemical end product is selected from the group consisting of glucose, cholesterol, fatty acids, and triglycerides.

16. (Original) The compounds of claim 15 wherein MPO_3^{2-} or $\text{MP}(\text{O})(\text{NHR}^6)\text{O}^-$ is an AMP activated protein kinase activator.

17. (Original) The compounds of claim 1 wherein Y is -O- located adjacent to the W' and W groups.

18. (Original) The compounds of claim 1 wherein Y is -O- located adjacent to the V group.

19. (Cancelled)

20. (Original) The compounds of claim 1 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

Patent
45198.00013.RCE2

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus.

21. (Original) The compounds of claim 20 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl; or

together V and W are connected via an additional 3 carbon atoms to form a cyclic substituted group containing 6 carbon atoms and mono-substituted with a substituent selected from the group consisting of hydroxyl, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

22. (Original) The compounds of claim 21 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

23. (Original) The compounds of claim 22 wherein Z, W, and W' are H; and R⁶ is selected from the group consisting of -H, and lower alkyl.

24. (Original) The compounds of claim 23 wherein V is selected from the group consisting of aryl and substituted aryl.

25. (Original) The compounds of claim 24 wherein V is selected from the group consisting of phenyl, and substituted phenyl.

26. (Original) The compounds of claim 25 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, and 3,5-difluorophenyl.

27. (Original) The compounds of claim 22 wherein V is selected from the group consisting of heteroaryl and substituted heteroaryl.

Patent
45198.00013.RCE2

28. (Original) The compounds of claim 27 wherein V is 4-pyridyl.

29. (Original) The compounds of claim 21 wherein together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and mono-substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

30. (Original) The compounds of claim 29 wherein together V and W form a cyclic group selected from the group consisting of $-\text{CH}_2\text{-CH(OH)-CH}_2-$, $-\text{CH}_2\text{CH(OCOR}^3\text{)-CH}_2-$, and $-\text{CH}_2\text{CH(OCO}_2\text{R}^3\text{)-CH}_2-$.

31. (Previously Amended) The compounds of claim 1 wherein V is -H, and Z is selected from the group consisting of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC(O)R}^3$, and $-\text{CHR}^2\text{OCO}_2\text{R}^3$.

32. (Original) The compounds of claim 22 wherein Z is selected from the group consisting of $-\text{OR}^2$, $-\text{SR}^2$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-(\text{CH}_2)_p\text{-OR}^{12}$, and $-(\text{CH}_2)_p\text{-SR}^{12}$.

33. (Original) The compounds of claim 32 wherein Z is selected from the group consisting of $-\text{OR}^2$, $-\text{R}^2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-(\text{CH}_2)_p\text{-OR}^{12}$, and $-(\text{CH}_2)_p\text{-SR}^{12}$.

34. (Original) The compounds of claim 33 wherein Z is selected from the group consisting of $-\text{OR}^2$, -H, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, and $-\text{NHCOR}^2$.

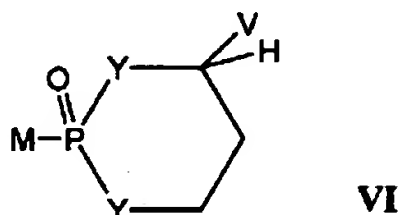
35. (Original) The compounds of claim 22 wherein W and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

36. (Original) The compounds of claim 35 wherein W and W' are the same group.

Patent
45198.00013.RCE2

37. (Original) The compounds of claim 36 wherein W and W' are H.

38. (Previously Amended) The compounds of claim 20 wherein said compound is of formula VI:



wherein

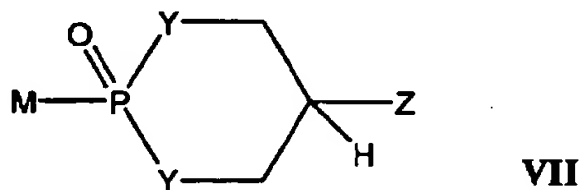
V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

39. (Original) The compounds of claim 38 wherein M is attached to phosphorus via an oxygen or carbon atom.

40. (Original) The compounds of claim 38 wherein V is selected from the group consisting of phenyl and substituted phenyl.

41. (Original) The compounds of claim 38 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, and 4-pyridyl.

42. (Previously Amended) The compounds of claim 20 wherein said compound is of formula VII:



wherein

Z is selected from the group consisting of:
-CHR²OH, -CHR²OC(O)R³, -CHR²OC(S)R³, -CHR²OCO₂R³, -CHR²OC(O)SR³,

Patent
45198.00013.RCE2

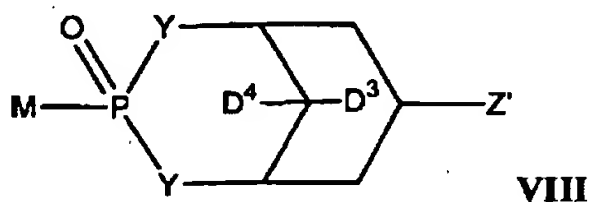
$-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, and $-\text{CH}_2\text{aryl}$.

43. (Original) The compounds of claim 42 wherein M is attached to the phosphorus via a carbon or oxygen atom.

44. (Original) The compounds of claim 43 wherein Z is selected from the group consisting of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, and $-\text{CHR}^2\text{OCO}_2\text{R}^3$.

45. (Original) The compounds of claim 44 wherein R^2 is $-\text{H}$.

46. (Previously Amended) The compounds of claim 20 wherein said compound is of formula VIII:



wherein

Z' is selected from the group consisting of $-\text{OH}$, $-\text{OC}(\text{O})\text{R}^3$, $-\text{OCO}_2\text{R}^3$, and $-\text{OC}(\text{O})\text{SR}^3$;

D^3 is $-\text{H}$;

D^4 is selected from the group consisting of $-\text{H}$, alkyl, $-\text{OH}$, and $-\text{OC}(\text{O})\text{R}^3$.

47. (Cancelled)

48. (Previously Amended) The compounds of claim 32 wherein W and W' are H, V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl, and Z is selected from the group consisting of $-\text{H}$, OR^2 , and $-\text{NHCOR}^2$.

49. (Original) The compounds of claim 48 wherein Z is $-\text{H}$, and M is attached to the phosphorus of formula I via an oxygen or carbon atom.

Patent
45198.00013.RCE2

50. (Previously Amended) The compounds of claim 49 wherein V is selected from the group consisting of phenyl and substituted phenyl.

51. (Original) The compounds of claim 49 wherein V is an optionally substituted monocyclic heteroaryl containing at least one nitrogen atom.

52. (Original) The compounds of claim 49 wherein M is attached via an oxygen atom.

53. (Original) The compounds of claim 51 wherein V is 4-pyridyl.

54. (Original) The compounds of claim 52 wherein MH is selected from the group consisting of LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC, ribavirin, penciclovir, 5-fluoro-2'-deoxyuridine, FIAU, FIAC, BHCG, 2'R,5'S(-)-1-[2-(hydroxymethyl)oxathiolan-5-yl]cytosine, (-)-b-L-2',3'-dideoxycytidine, (-)-b-L-2',3'-dideoxy-5-fluorocytidine, FMAU, BvaraU, E-5-(2-bromovinyl)-2'-deoxyuridine, Cobucavir, TFT, 5-propynyl-1-arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'-deoxyguanosine, Cytallene, Oxetanocin A, Oxetanocin G, Cyclobut A, Cyclobut G, fluorodeoxyuridine, dFdC, araC, bromodeoxyuridine, IDU, CdA, F-ara-A, 5-FdUMP, coformycin, and 2'-deoxycoformycin.

55. (Original) The compounds of claim 52 wherein MH is selected from the group consisting of ACV, GCV, 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, and (R)-9-(3,4-dihydroxybutyl)guanine.

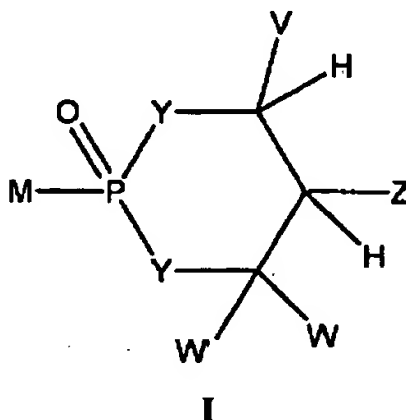
56. (Original) The compounds of claim 49 wherein M is attached to the phosphorus via a carbon atom.

57. (Original) The compounds of claim 56 wherein V is selected from the group consisting of phenyl and 4-pyridyl and MH is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMMA, FPMMA, and PMPA.

58. – 149. (Cancelled)

150. (Previously Amended) A method of making a compound of Formula I comprising,

a) transforming a drug having a $-\text{PO}_3^{2-}$ or $-\text{P}(\text{O})(\text{NHR}^6)\text{O}^-$ moiety into a compound of formula I:



wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Patent
45198.00013.RCE2

Z is selected from the group consisting of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2_2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p-\text{OR}^{12}$, and $-(\text{CH}_2)_p-\text{SR}^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-\text{R}^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

one Y is -O- and the other Y is $-\text{NR}^6-$;

M is selected from the group that attached to PO_3^{2-} , $\text{P}_2\text{O}_6^{3-}$, $\text{P}_3\text{O}_9^{4-}$, or $\text{P}(\text{O})(\text{NHR}^6)\text{O}^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not $-\text{NH}(\text{lower alkyl})$, $-\text{N}(\text{lower alkyl})_2$, $-\text{NH}(\text{lower alkylhalide})$, $-\text{N}(\text{lower alkylhalide})_2$, or $-\text{N}(\text{lower alkyl})(\text{lower alkylhalide})$; and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

151. (Previously Amended) The method of claim 150 further comprising,

a) converting M-PO_3^{2-} to a compound $\text{M-P}(\text{O})\text{L}''_2$ wherein L'' is a halogen; and

b) reacting $\text{M-P}(\text{O})\text{L}''_2$ with $\text{HY-CH(V)CH(Z)-CW(W')-YH}$.

152. (Original) The method of claim 151 wherein $\text{HY-CH(V)CH(Z)-CW(W')-YH}$ is chiral.

153. (Original) The method of claim 152 further comprising isolating a single diastereomer.

Patent
45198.00013.RCE2

154. (Cancelled)

155. (Previously Amended) The method of claim 166 wherein
L-P(-YCH(V)CH(Z)-CW(W')Y-) is chiral.

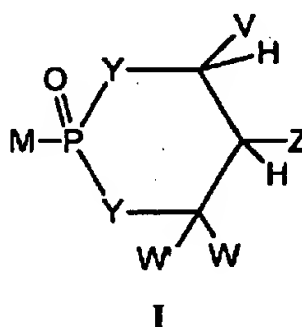
156. (Original) The method of claim 155 wherein the chiral phosphoramidite is generated using a
chiral amino alcohol.

157. (Original) The method of claim 155 wherein said oxidizing agent produces a single
stereoisomer at the phosphorus.

158. – 164. (Cancelled)

165. (Previously Amended) The compounds of claim 1 wherein V and M are *cis* to one another
on the phosphorus-containing ring of Formula I.

166. (Previously Added) The method of making a compound of formula I:



comprising

a) converting a hydroxyl or amino on M to a phosphoramidite by reaction with L-P(-YCH(V)CH(Z)-CW(W')Y-) wherein L selected from the group consisting of NR¹₂ and halogen; and

b) transforming said phosphoramidite into a compound of formula I by reaction with an
oxidizing agent;

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl,
alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and
1-alkynyl; or

Patent
45198.00013.RCE2

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2_2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p-\text{OR}^{12}$, and $-(\text{CH}_2)_p-\text{SR}^{12}$;

p is an integer 2 or 3;

with the provisos that:

- a) V, Z, W, W' are not all -H; and
 - b) when Z is $-\text{R}^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;
- each R^1 is independently selected from the group consisting of alkyl, aryl, and aralkyl or together R^1 and R^1 form a cyclic group, optionally containing a heteroatom;
- R^2 is selected from the group consisting of R^3 and -H;
- R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;
- R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

Patent
45198.00013.RCE2

R^{12} is selected from the group consisting of -H, and lower acyl;
one Y is -O- and the other Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-} , $P_2O_6^{3-}$, $P_3O_9^{4-}$, or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

- 1) M is not $-NH(\text{lower alkyl})$, $-N(\text{lower alkyl})_2$, $-NH(\text{lower alkylhalide})$, $-N(\text{lower alkylhalide})_2$, or $-N(\text{lower alkyl})(\text{lower alkylhalide})$;
- 2) R^6 is not lower alkylhalide; and
- 3) R^1 is not methyl.

167. - 170. (Cancelled)

171. (Previously Added) The compounds of claim 1, wherein:

W and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2\text{aryl}$, $-CH(\text{aryl})OH$, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH\text{aryl}$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

p is an integer 2 or 3;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H and lower acyl;

Patent
45198.00013.RCE2

one Y is -O- and the other Y is -NR⁶-;

M is selected from the group that attached to PO₃²⁻, P₂O₆³⁻, P₃O₉⁴⁻ or P(O)(NHR⁶)O⁻ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not -NH(lower alkyl), -N(lower alkyl)₂, -NH(lower alkylhalide), -N(lower alkylhalide)₂, or -N(lower alkyl) (lower alkylhalide); and

2) R⁶ is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

172. (Previously Added) The compounds of claim 1, wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl;

Z is selected from the group consisting of -CHR²OH, -CHR²OC(O)R³, -CHR²OC(S)R³, -CHR²OC(S)OR³, -CHR²OC(O)SR³, -CHR²OCO₂R³, -CH₂aryl, -CH(aryl)OH, -CH(CH=CR²)OH, -CH(C≡CR²)OH, -SR², and -CH₂NHaryl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R⁶ is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

one Y is -O- and the other Y is -NR⁶-;

M is selected from the group that attached to PO₃²⁻, P₂O₆³⁻, P₃O₉⁴⁻ or P(O)(NHR⁶)O⁻ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not -NH(lower alkyl), -N(lower alkyl)₂, -NH(lower alkylhalide),

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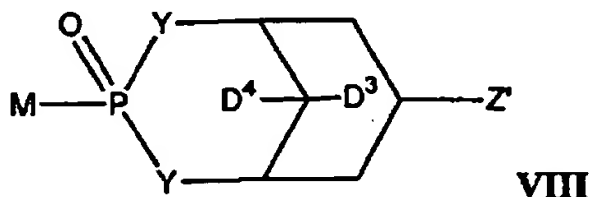
Patent
45198.00013.RCE2

-N(lower alkylhalide)₂, or -N(lower alkyl) (lower alkylhalide); and

2) R⁶ is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

173.(Previously Amended) The compounds of claim 1 that are of formula VIII:



wherein:

Z' is selected from the group consisting of -OH, -OCO₂R³, -OC(O)R³, and -OC(O)SR³;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R⁶ is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

one Y is -O- and the other Y is -NR⁶-;

D³ is -H;

D⁴ is selected from the group consisting of -H, alkyl, -OH, -OR² and -OC(O)R³.

M is selected from the group that attached to PO₃²⁻, P₂O₆³⁻, P₃O₉⁴⁻ or P(O)(NHR⁶)O⁻ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

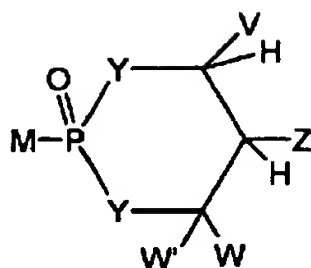
1) M is not -NH(lower alkyl), -N(lower alkyl)₂, -NH(lower alkylhalide), -N(lower alkylhalide)₂, or -N(lower alkyl) (lower alkylhalide); and

2) R⁶ is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

Patent
45198.00013.RCE2

174. (New) A compound of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$,

Patent
45198.00013.RCE2

$-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$,
 $-(\text{CH}_2)_p-\text{OR}^{12}$, and $-(\text{CH}_2)_p-\text{SR}^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-\text{R}^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

one Y is -O- and the other Y is $-\text{NR}^6$;

M is a nucleoside that attached to PO_3^{2-} , $\text{P}_2\text{O}_6^{3-}$, $\text{P}_3\text{O}_9^{4-}$ or $\text{P}(\text{O})(\text{NHR}^6)\text{O}^-$ is a biologically active agent but is not an FB Pase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the proviso that R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.